PSJ2 Exh 5

File Provided Natively

Chronic Pain: Prevalence and Impact

- 34 million Americans
- $65 - $75 billion per year
- 50 million lost work days

Perceived Adequacy of Education

	About Controlled Substances Requirements	About Opioids and Pain Management
Poor	24 (5)	64 (12)
Fair	151(28)	197 (38)
Good	266 (49)	229 (44)
Excellent	97 (18)	34 (7)

Columns may not total 100% due to rounding.

Perceptions of Legality and Medical Acceptability of Extended Prescribing/Dispensing of Opioids

Response	Chronic Cancer Pain[a]	Chronic Cancer Pain with History of Opioid Abuse	Chronic Noncancer Pain	Chronic Noncancer Pain with History of Opioid Abuse
	No. (%)	No. (%)	No. (%)	No. (%)
Lawful and generally acceptable medical practice	488 (93)	336 (61)	299 (57)	43 (8)
Lawful but generally not acceptable medical practice that should be discouraged	7 (1)	92 (17)	159 (30)	249 (47)
Violation of federal or state controlled substances or medical practice laws or regulations that should be investigated	13 (2)	34 (6)	33 (6)	184 (35)
Don't know	17 (7)	65 (12)	34 (7)	50 (10)

Columns may not total 100% due to rounding.

American Pain Society Study

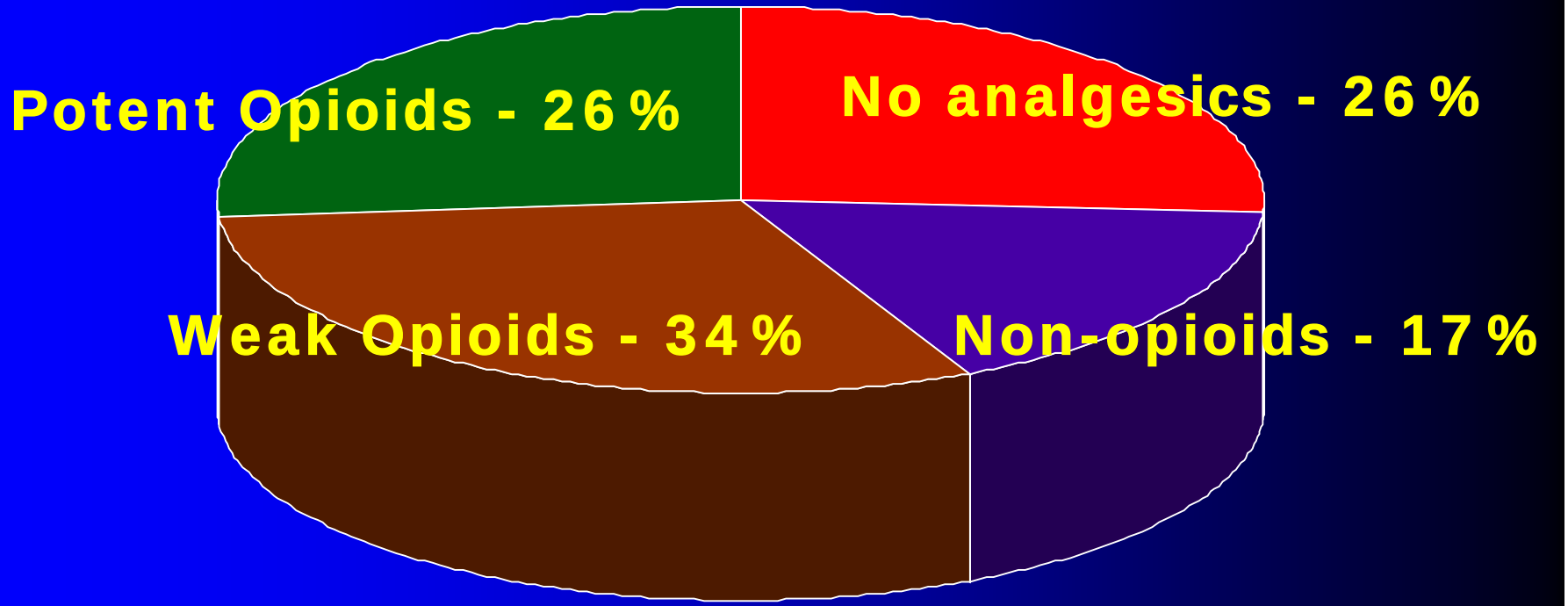
- N= 2642 patients with at least 6 months of constant or chronic pain of moderate to severe intensity, not due to cancer
- 56% had been suffering for more than 5 years
- 41% felt that their pain was out of control
- 94% sought a physician's care for pain
- 47% changed physicians at least once
- 22% switched three or more times

The major reasons for changing doctors were:

- continued suffering (42%)
- lack of physician knowledge about pain (31%)
- not having their pain taken seriously by the treating physician (29%)
- doctors' lack of aggressiveness in treating pain (27%)

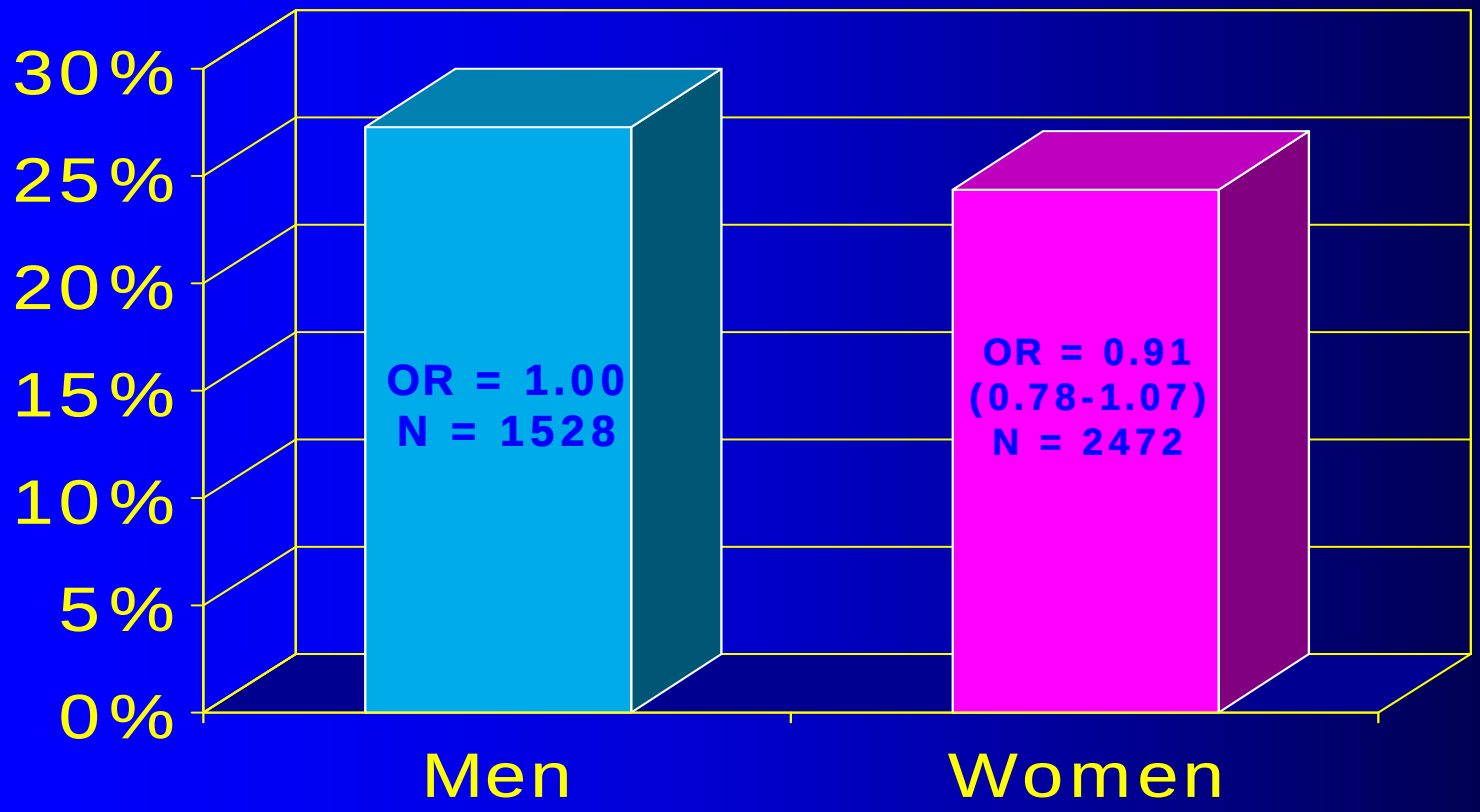
Management of Pain in Elderly Patients with Cancer

N= 13,625



R. Bernabei, G. Gambassi, K Lapane, et al
JAMA 1998;279:1877-1882

No Analgesics by Gender



National Survey on Chronic Pain

- Of those with pain ≥5/10, nearly half said their pain is "out of control"
- Of those with pain ≥9/10, 30% switched physicians ≥3 times because:
  - Ignorance of physician re pain - 31%
  - Physician didn't take pain seriously - 29%
  - Failure to treat pain aggressively - 27%

Pharmacotherapy for Pain

Categories of Analgesic Drugs

- Opioid analgesics
- Nonopioid analgesics
- Adjuvant analgesics
- Drugs for headache

Barriers to Opioid Therapy

- Patient-related factors
  - stoicism, fear of addiction
- System factors
  - fragmented care, lack of reimbursement
- Clinician-related factors
  - Poor knowledge of pain management, opioid pharmacology, and chemical dependency
  - Fear of regulatory oversight

Negative Consequences of Unrelieved Pain: Patient

- Depression
- Anxiety
- Fatigue
- Sleep disturbances
- Decreased functional status
- Decreased quality of life

Negative Consequences of Unrelieved Pain: Family Caregiver

- Depression
- Anxiety
- Fatigue
- Sleep disturbances
- Decreased functional status
- Decreased quality of life
- Increased caregiver burden

Evolving Role of Opioid Therapy

- From the 1980's to the present:
  - More pharmacological interventions for acute and chronic pain
  - Changing perspectives on the use of opioid drugs for chronic pain

Evolving Role of Opioid Therapy

- Historically, opioids have been emphasized in medical illness and de-emphasized in nonmalignant pain

Opioid Therapy in Pain Related to Medical Illness

Opioid therapy is the mainstay approach for

- Acute pain
- Cancer pain
- AIDS pain
- Pain in advanced illnesses

But undertreatment is a major problem

Opioid Therapy in Chronic Nonmalignant Pain

Undertreatment is likely because of

- Barriers (patient, clinician, and system)
- Published experience of multidisciplinary pain programs
  - Opioids associated with poor function
  - Opioids associated with substance use disorders and other psychiatric disorders
  - Opioids associated with poor outcome

Opioid Therapy in Chronic Nonmalignant Pain

- There is increasing use of long-term opioid therapy in diverse pain syndromes
  - Slowly growing evidence base
  - Acceptance by pain specialists
  - Reassurance from the regulatory and law enforcement communities

Opioid Therapy in Chronic Nonmalignant Pain

- Supporting evidence

  >1000 patients reported in case series and surveys

- Small number of RCT's

Positioning Opioid Therapy

- Consider as first-line for patients with moderate to severe pain related to cancer or AIDS, or another life threatening illness
- Consider for all patients with moderate to severe non-cancer pain, but weigh the influences
  - What is conventional practice?
  - Are opioids likely to work well?
  - Are there reasonable alternatives?
  - Are drug-related behaviors likely to be responsible, or problematic and requiring intensive monitoring

Opioid Therapy: Needs and Obligations

- Learn how to assess patients with pain and make reasoned decisions about a trial of opioid therapy
- Learn prescribing principles
- Learn principles of addiction medicine sufficient to monitor drug-related behavior and address aberrant behaviors

Opioid Therapy: Prescribing Principles

- Prescribing principles
  - Drug selection
  - Dosing to optimize effects
  - Treating side effects
  - Managing the poorly responsive patient

Adverse Physiological Sequelae of Pain

- **Increased catabolic demands**
  - •Muscle breakdown
  - •Poor healing
  - •Weakness
- **Impaired respiratory effort**
  - • Risk of atelectasis, pneumonia
- **Impaired limb movement**
  - • Risk of thromboembolic events
- **Water retention**
- **Inhibited GI motility**
- **Hypertension, tachycardia, and tachypnea (acute)**

Adverse Psychological Sequelae of Pain

- **Negative emotions**
  - Anxiety
  - Depression
- **Sleep deprivation**

Existential suffering

Adverse Immunological Sequelae of Pain

- **Impaired immune response**
  - Decreased natural killer (NK) cells

Fear of Dependence

- A physical or pharmacological phenomenon characterized by an abstinence syndrome upon abrupt drug discontinuation, substantial dose reduction, or administration of an antagonist.
- Dependence is nearly universal among patients receiving continual opioid therapy for a week or more.
- Opioids can be discontinued in dependent patients without withdrawal difficulties by simply tapering them over about a week.

Fear of Addiction

- Characterized by loss of control over drug use and compulsive use of the drug despite harm from that use.
- Iatrogenic addiction from opioid analgesia in patients experiencing pain is exquisitely rare. The Boston Collaborative Drug Surveillance Program study revealed only four cases of iatrogenic addiction among 11,882 patients without a prior history of substance abuse who received opioids for a broad range of indications.

Fear of Tolerance

- Three types of tolerance occur with opioids.
  - Tolerance to centrally mediated effects, i.e., respiratory and CNS depression, normally occurs within 5 to 7 days of continuous administration of regularly scheduled opioids.
  - Tolerance to the constipating effects of opioids does not occur. Activated mu opioid receptors in the colon inhibit peristalsis.
  - Increases in opioid doses may be required over the first few days or weeks of therapy during titration to response. Tolerance to opioid analgesia typically does not occur once an effective dose of opioid is identified and administered regularly.

Other Patient Fears

- Some patients may believe that parenterally administered opioids are more effective than analgesics administered by the transdermal, oral or other noninvasive routes. However, once an opioid occupies a receptor, activity will occur regardless of how the medication was administered.
- For other patients, the use of the parenteral route can signal advancing disease and may be a psychological disadvantage.

General Principles of Pharmacologic Management - 1

- Individualize the dosing regimen.
- Titrate to maximal effect with minimal side effects.
- Administer medications ATC.
- Use the least invasive route possible.

General Principles of Pharmacologic Management - 2

- Use appropriate combination based on mechanism of action.
- Use the simplest regimen possible to avoid polypharmacy.
- Anticipate and treat the side effects of medications.
- Reassess the effectiveness of the plan.

Patient & Family Caregiver Education and Coaching - 1

- Obtaining analgesic medications
  - Financial constraints
  - Pharmacy issues
- Obtaining information about analgesics
  - Lack of education
  - Inaccurate information

Patient & Family Caregiver Education and Coaching - 2

- Maintaining an optimal analgesic regimen
  - Most efficacious analgesic
  - Management of breakthrough pain
  - Optimal timing of analgesics
- Management of side effects
- Problems with cognition

Patient & Family Caregiver Education and Coaching - 3

- Management of new or unusual pain problems
- Management of multiple symptoms
  - Treatment-related symptoms
  - Disease-related symptoms
  - Symptoms associated with concurrent medical problems

Drug Regulation

- Federal and state laws provide three categories of control to regulate *over the counter* drugs, *prescription* drugs, and *controlled substances*.
- **Controlled substances** include prescription drugs and illegal drugs that have a potential for abuse and a potential for producing psychological or physical dependence.

Controlled Substances Act

(21 USC 801, et seq. & 21 CFR 1301, et seq.)

- According to the federal CSA, in order for a prescription to be valid, it:

  -must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of professional practice.

Source: Controlled Substances Act [21 C.F.R. 1306.04(a)]

Federation of State Medical Boards of the United States

- Model Guidelines for the Use of Controlled Substances for the Treatment of Pain
- Developed jointely by DEA and FSMB
- Adopted May 2, 1998

Source: FSMB of US Guidelines. 1998

FSMB Model Guidelines

Pain Management Policy (cont.)

Guidelines for evaluating use of controlled substances for pain control:

- √ **Evaluation of the patient:** Complete medical history & physical exam
- √ **Treatment Plan:** Written plan; state objectives and proposed treatments & medications
- √ **Informed Consent & Agreement for Treatment:** Discuss risks and benefits of use of controlled substances. Written agreement advised if substance abuse is suspected. Physician may include urine/serum screenings, number & frequency of Rx refills, and reasons for discontinuation of drug therapy (e.g..,violation of agreement, positive drug screen, too many "lost" prescriptions/medications, etc.)
- √ **Periodic Review:** At reasonable intervals evaluate case and patients' compliance with treatment plan and reevaluate appropriateness of continued treatment
- √ **Consultation:** Physician should be willing to refer patient, as necessary, for additional evaluation and treatment in order to achieve treatment objectives
- √ **Medical Records:** Accurate and complete records reflecting all of the above items
- √ **Compliance with Controlled Substances Laws and Regulations:** As described in DEA's *Physicians Manual,* the CSA, & applicable state regulations

DAWN Mentions of Fentanyl

- January 1996 to June 1998 (30 months): total of **52** fentanyl mentions* out of approximately **2.4** million DAWN drug mentions in US
- 23 of 52 episodes involved only Fentanyl
- Fentanyl in combination with alcohol found in 31% of cases

**Injectable and illicit fentanyl (China White) believed to account for most, if not all, DAWN fentanyl mentions*

Allay Fears About Addiction

- Distinguish between physical dependence and addiction
- Explain measures for preventing and monitoring for addiction
- Obtain informed consent
- Use a written contract

Set Realistic Expectations

- Expect reduction of pain, not cure
- Side effects
  - Rare: respiratory depression, chronic sedation and cognitive blunting, addiction
  - Infrequent: persistent nausea, urinary retention, pruritus, vivid dreams
  - Frequent: constipation, physical dependence
- Involve family

Addiction/Diversion Potential

Minimize potential by prescribing agents with:

- Gradual onset
- Using more secure delivery systems
- Using less frequently abused preparations

Some Obstacles to Pain Management

- 1998: In response to Oregon referendum on physician-assisted suicide, Congress introduced *Lethal Drug Abuse Prevention Act of 1998* that, among other things, would authorize DEA to suspend or revoke DEA registrations in cases of physician-assisted suicide;
- Bill received bipartisan support but failed to come to a vote in 105th Congress because of Presidential impeachment proceedings.
- June 1999: Bill reintroduced in the 106th Congress as *Pain Relief Promotion Act*. Senate version attracts 42 cosponsors, including Senators Joseph I. Lieberman (D-CT) and Senate Majority Leader Trent Lott (R-MS).

Source: Congressional Record

Some Obstacles to Pain Management
(Cont.)

- May 23, 2000 *Pain Relief Promotion Act of 2000* (S. 2607) introduced to full Senate by Sen. Ron Wyden (D-OR)
- Sen. Wyden opposed Act, saying that PRPA "*may, in fact, have chilling effect on physicians' pain management, thus actually increasing suffering at the end of life.*"
- Although prohibiting assisted suicide, Act states that burden for proving practitioner's intent to cause death must be established by **"clear and convincing evidence,"** and **not** by showing that registrant knew that use of controlled substances would increase the risk of death.

Source: Congressional Record

Some Obstacles to Pain Management
(Cont.)

- Sen. Wyden listed thirty organizations with expertise in pain management and palliative care that are opposed to the Pain Relief Promotion Act.
- Sen. Wyden quoted several pain experts, including:
  - Dr. Kathleen M. Foley: *"In short, the underpinnings of this legislation are not based on scientific evidence. It would be unwise to institutionalize the myth into law that pain medications hasten death."*
- September 19, 2000 - a *Washington Post* editorial opposed *Pain Relief Promotion Act* and noted the "division in the medical community" over some of the Bill's provisions.

Source: Congressional Record & The Washington Post, 9/19/00

Some Obstacles to Pain Management (Cont.)

- 1996 CA poll of MDs found that 69 percent cited "fear of potential disciplinary action from government regulators" as reason for conservative pain management (Portenoy. J. of Pain & Symptoms Mgmt. 1996)
- 1998: study reported in JAMA stated that 50 to 90 percent of elderly cancer patients suffer unrelieved pain (JAMA 1998; 279: 1877-1882)

Source: as indicated

Some Obstacles to Pain Management
(Cont.)

- On April 25, 2000, Dr. Kathleen Foley, program director for clinical pain management and research at New York's Sloan-Kettering Cancer Center, testifying before the Senate Judiciary Committee on the subject of the *Pain Relief Promotion Act*, stated that:

  Physician surveys by the New York State Department of Health have shown that a strict regulatory environment negatively impacts physician prescribing practices and leads then to intentionally undertreat patients because of concern of regulatory oversight.

Some Obstacles to Pain Management
(Cont.)

- A contrary view is held by F. Michael Gloth III, MD, Johns Hopkins University School of Medicine:
  - State of Maryland has enacted legislation very similar to the proposed federal PRPA;
  - Impact on physician-assisted suicide has been *imperceptible;*
  - Law provides specific wording to protect clinicians who prescribe medication for pain relief;
  - Data suggest that states with such laws may actually experience increased opioid use.

Potter, JAMA 283:22, June 14, 2000

Some Obstacles to Pain Management
(Cont.)

- Multiple Copy Prescription Program (MCPP) often cited as reason for conservative pain management:
- *"MCPP status is a strong influence in predicting the type of analgesic used…the presence of a state MCPP exerts a negative influence on the probability that a Schedule II analgesic will be prescribed in an office visit, and a strong positive effect on the probability of Schedule III opioid analgesic receipt…If rates of use of Schedule II medications are indeed lower in the MCPP states, patients in those states may experience greater levels of pain than their counterparts in non-MCPP states."*

Source: Wastila & Bishop, J of Pharm Care Pain Symptom Control. 1996; 4(3):3-19

Multiple Copy Prescription Program Contrary View

- **"Chilling effect"** of MCPP disputed by DEA & National Alliance for Model State Drug Laws
- *Quantity of fentanyl produced in 1998 is eight times what it was in 1990. Oxycodone, hydromorphone and hydrocodone production have tripled since 1990, while morphine production has more than doubled during same period. ARCOS reports for 1997-1998 reflect a rise in overall consumption of oxycodone, hydrocodone, hydromorphone, methadone, morphine and fentanyl.*

State & Federal Sanctions

- Pain management practice is high risk area for attracting substance abusers, doctor shoppers, prescription forgers, and others seeking to unlawfully obtain controlled substances
- State & Federal regulators attracted to pain management practice because potential for criminal diversion of controlled substances is highest with this category of practice
- Nonetheless, intervention by regulators generally overestimated in terms of numbers of official sanctions

Perceived Legality of Opioid Use: Survey of State Medical Board Members

Acceptability of Opioid Use	Legal/ Acceptable	Legal/Not Acceptable	Illegal/ Investigate	Don't Know
Cancer pain	75	14	5	7
Cancer pain + substance abuse	46	22	14	16
Chronic nonmalignant pain	12	47	32	7
Chronic nonmalignant pain + substance abuse	1	25	58	6

Defining the Problems

- Fear of iatrogenic addiction
- Misunderstanding of what addiction is
- Management strategies for patients with different substance abuse-related problems

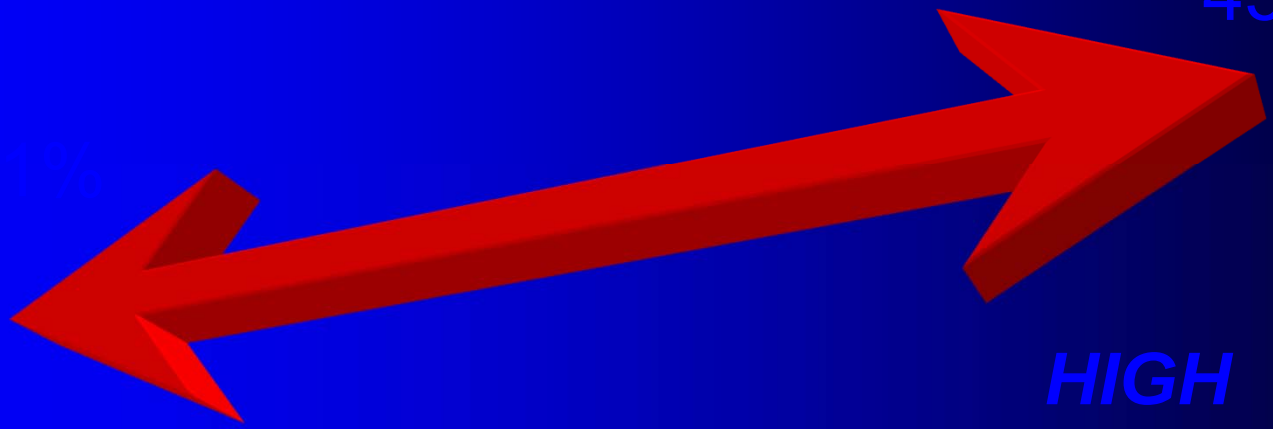
What is the Risk of Addiction and Aberrant Behavior?

- Boston Collaborative Drug Surveillance Project: Porter and Jick, 1980. *NEJM*.
  - 4 cases of addiction in 11,882 patients with no prior history of abuse who received opioids during inpatient hospitalization

- Dunbar and Katz, 1996. *JPSM*.
  - 20 patients with ***both*** chronic pain and substance abuse problems on chronic opioid therapy
  - Nine out of 20 abused medication
  - Of the 11 who did not abuse the medications, all

Spectrum of Risk of Addiction or Aberrant Behavior

~ 45%



HIGH

Long-term exposure to opioids in addicts,

Dunbar and Katz

Where is your patient?

- Addiction or aberrant behavior results from a combination of
  - Chemical
  - Psychiatric
  - Social
  - Familial
  - Genetic

Influences

Consider the Risk of Not Treating Pain in Addicts

- Passik, et al. 2001.

- Study comparing addicts with AIDS to cancer patients and their response to under-treatment
  - Aberrant behavior is set in motion by under-treatment

Long-Acting Opioids Have Lower Street Value

Medication	Street Value* ($)
Hydromorphone	47.00 ± 25.00
Slow-release morphine	3.00 ± 3.00
Diazepam	7.00 ± 3.00

*Participants who reported having used or brought the drug

Brookoff D. *J Gen Intern Med.* 1993;8:688-690